

Table 4. Comparison of Intermediate Tier Functional and Selected ToxCast HTS Assay Findings.

Compound/ Descriptor	Rat Aortic Explant	Rat Whole Embryo	Zebrafish Embryo	Bioseek ToxCast HTS Assay Subset	Tanguay ZF ToxCast HTS Assay Subset	NHEERL ZF 144hpf_ TERATOSCORE_up
Assay Contribution to Embryonic Vascular Disruption MoA	3-D ex vivo primary culture, microvessel outgrowth (reflective of angiogenesis)	Intact organism, embryonic and vascular development (including placental)	Intact organism, embryonic and vascular development (chorion-on)	Human primary cell co-cultures, includes molecular regulators endpoints for vasculogenesis and angiogenesis	High throughput intact zebrafish developmental assay (dechorionated)	Medium throughput intact zebrafish developmental assay (chorion-on)
5HPP-33 Response Potency (μM)	1.28	21.2	3.41	Minimum AC50 = 2.90 25th Percentile = 10.87 Median AC50 = 15.2	Active in two assay endpoints. AC50 = 26.2 (Increased mortality), 27.1 (Activity score)	4.44
Outcome Summary	Disorganized/degenerate microvessel outgrowth	Embryo lethality	Embryo lethality	Broad activity, anti-proliferative to endothelial cells, cell-cell signaling effects	Embryo lethality, decreased activity	Embryo lethality
TNP-470 Response Potency (μM)	0.018	0.038	0.032	Minimum AC50 = 0.001 25th Percentile = 0.45 Median AC50 = 6.2	Minimum AC50 = 0.003 25% Percentile = 0.009 Median AC50 = 0.026	Not active
Outcome Summary	Stunted microvessel outgrowth, otherwise normal morphology	Dysmorphogenesis, primarily caudal extension defects and abnormal somite patterning	Dysmorphogenesis, primarily caudal extension defects and abnormal somite patterning	Anti-proliferative to endothelial cells, T cells and fibroblasts. Anti-inflammatory, immunomodulatory, and tissue remodeling activity.	Dysmorphogenesis: Caudal fin, axial, pericardial edema, yolk sac defects, eye and jaw defects	Not active